REMARKS

Applicants appreciate the notification of allowable subject matter, i.e. that claims 39-68 are merely objected to are allowable if written independent form.

Applicants also note that only two claims have been rejected over prior art.

Claims 1-3, 7-10, 13, 15, 17, 19-20, and 22 have been amended. No new matter has been added by the claim amendments. Support for the amendment to claims can be found in the claims as originally filed and throughout the specification.

Claims 1-38 were rejected under 35 U.S.C. § 112, second paragraph for formality-type matters. The rejection is traversed.

The Examiner has rejected claims for containing the terms "including," "containing" or "contain." The word "including" has been removed from the claims. With regard to the terms "containing" or "contain" applicants respectfully traverse the Examiner's rejection. At each occurrence these terms serve to require that claimed heterocyclic groups contain at least one heteroatom selected from N, O, and S.

The language "...heterocyclic groups containing one or more heteroatom(s)..." is clearly understood by persons skilled in the art, particularly upon consideration of the supporting specification, as is proper. For instance, as recited by the specification and even the claims themselves, a heterocycle comprises at least one ring atom selected from N, O and S. See, for example, page 25, line 19 to page 26, line 5 for a discussion of the term "heterocyclic group." Moreover, the specification provides an extensive listing of exemplary heterocyclic groups at page 26, lines 6-27.

Claim language that allowed alkyl groups to optionally have one or more double or triple bonds has been amended. Alkenyl and alkynyl groups are now separately cited in the claims.

Applicant's note that these amendments reciting alkenyl and alkynyl groups do not change the scope of the claims.

Variables R_X and R_Y as recited in claims 14-17 are fully supported by the specification. See, for example, pages 8-11 and page 14 of the application.

The meaning of the term "stress-related disorder" is discussed in the application. See, for example, page 19, lines 21-23 of the application. This term is also well-understood in the art.

In view thereof, reconsideration and withdrawal of the rejection are requested.

Claims 27 and 36 were rejected under 35 U.S.C. § 112, first paragraph. As grounds for the rejection, the position is taken that (page 3 of the Office Action):

> The specification does not define the term "stress-related disorder", and does not provide any bioassay to show the activity of the claimed compounds for such disorder.

The rejection is traversed.

The application fully satisfies the requirements of 35 U.S.C. §112, including the requirements of Section 112, first paragraph.

The Examiner has indicated that he believes undue experimentation would be required to use the claimed compounds to treat stress-related disorders. The Examiner also alleges that the term "stress-related disorders" include "disorders such as diabetes, cardiovascular, myocardial, infarct, etc." Applicants are unaware that diabetes is a considered a stress-related disorder and there is no mention of this disease in the instant application. Instead the application provides a discussion of the term "stress-related disorder" at page 19, lines 21-23.

Applicants respectfully submit that CRF receptor antagonists were well known in the art at the time the application was filed to be useful for treating stress-related disorders. Furthermore the literature provides examples of how CRF receptor antagonists may be used to treat stress-related disorders. The specification also teaches how the compounds disclosed therein may be used to treat stress related disorders. See, for example, the "Pharmaceutical Preparations" section beginning on page 27 of the specification.

Furthermore, absolutely no reasons have been presented in the Action to establish why one skilled in the art could not make and use the claimed subject matter based on Applicants' disclosure. Such a basis for rejection under Section 112, first paragraph is simply not proper. It is well established that in the absence of any evidence why a supporting disclosure is not sufficient, the mere allegation of inadequacy is not considered to constitute a satisfactory basis for rejection under Section 112, first paragraph. See, for instance, the Manual of Patent Examining Procedure at Section 2164.04 which states (quoting *In re Marzocchi*):

> [I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

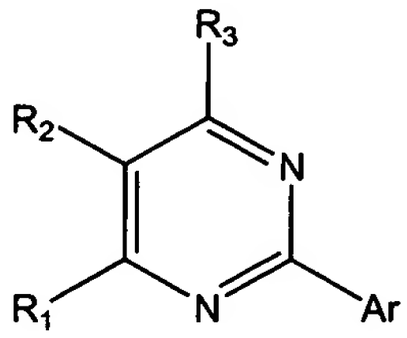
In view thereof, reconsideration and withdrawal of the rejection are requested.

Claims 1 and 2 were under 35 U.S.C. §102(e) over Murata et al. (U.S. Patent 5,972,946). The Murata et al. document is cited only for an isolated table of intermediate compounds at column 29 of the document. The rejection is traversed.

At that cited table of intermediates, the Murata et al. document reports certain compounds that have a 2-phenyl-**4-chloro**-pyrimidine structure, which at the 4 and optionally at the 6 position is substituted with one or two chloro groups and which at the 5-position is substituted by

groups of hydrogen, methyl, ethyl, nitro, COOEt, or the 5-position is part of a fused 6-membered ring. See Murata et al. Table 11, column 29.

In contrast, Applicants' amended claims 1 and 2 and call for compounds of the following formula:



wherein **the 4-ring position and the 6-ring position (i.e., R_4 and R_6) are not chloro**, and wherein the 5-ring position (i.e. R_2) is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted aminoalkyl, optionally substituted mono or dialkylamino, optionally substituted alkylthio, optionally substituted alkylsulfinyl, optionally substituted alkylsulfonyl, optionally substituted mono or dialkylcarboxamide, optionally substituted carbocyclic aryl or optionally substituted heteroaryl having from 1 to 3 rings, and 3 to 8 ring members in each ring and 1 to about 3 heteroatoms

The Murata et al. document does not disclose such substitution. Accordingly, the rejection should be withdrawn. See, for instance, *In re Marshall*, 198 USPQ 344, 346 ("[r]ejections under 35 USC 102 are proper only when the claimed subject matter is identically disclosed or described in the prior art.").

It is believed the application is in condition for immediate allowance, which action is earnestly solicited.

Respectfully submitted,

Date: April 29, 2002

By: _____

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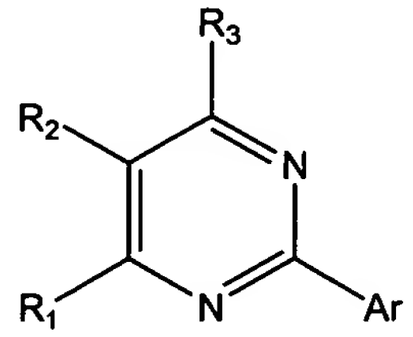
VERSION WITH CHANGES MARKED

(Additions are underlined; deletions are bracketed.)

1. (amended) A compound of the formula:



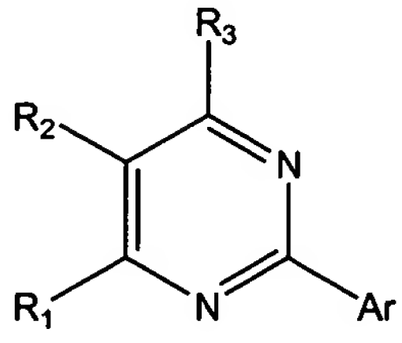
or a pharmaceutically acceptable salt thereof, wherein:

Ar is phenyl, 1- or 2-naphthyl, each of which is mono-, di-, or tri-substituted or mono-, di-, or tri-substituted heteroaryl having from about 5 to about 7 ring members and 1 to about 4 heteroatoms in the ring, the heteroatoms independently selected from the group consisting of N, O and S;

R_1 and R_3 are independently chosen from hydrogen, [halogen]<u>bromo, fluoro, iodo</u>, cyano, nitro, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted (cycloalkyl)alkyl, optionally substituted alkylthio, optionally substituted alkylsulfinyl, optionally substituted alkylsulfonyl, or optionally substituted mono- or dialkylcarboxamide, with the proviso that R_1 and R_3 are not both hydrogen; and

R_2 is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted aminoalkyl, optionally substituted mono or dialkylamino, optionally substituted alkylthio, optionally substituted alkylsulfinyl, optionally substituted alkylsulfonyl, optionally substituted mono or dialkylcarboxamide, optionally substituted carbocyclic aryl or optionally substituted heteroaryl having from 1 to 3 rings, and 3 to 8 ring members in each ring and 1 to about 3 heteroatoms.

2. (amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

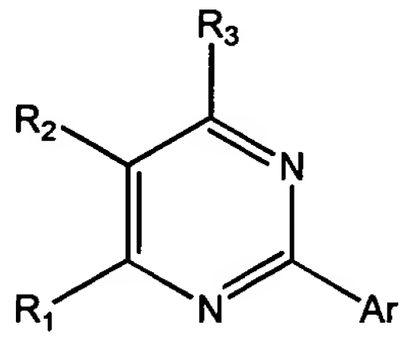
Ar is phenyl which is mono-, di-, or tri-substituted;

R_1 and R_3 are independently chosen from hydrogen, [halogen]bromo, fluoro, iodo, cyano, nitro, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted (cycloalkyl)alkyl, optionally substituted alkylthio, optionally substituted alkylsulfinyl, or optionally substituted alkylsulfonyl, and optionally substituted mono or dialkylcarboxamide, with the proviso that R_1 and R_3 are not both hydrogen; and

R_2 is optionally substituted alkyl, optionally substituted alkoxy, optionally substituted aminoalkyl, optionally substituted mono or dialkylamino, optionally substituted alkylthio, optionally substituted alkylsulfinyl, optionally substituted alkylsulfonyl, optionally substituted mono or dialkylcarboxamide, or

R_2 is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrimidinyl, pyridizinyl, and thiophenyl, each of which is optionally mono-, di-, or tri-substituted.

3. (amended) A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein:

R_1 and R_3 are independently selected from hydrogen, [halogen]bromo, fluoro, iodo, cyano, C_{1-6} alkyl$_{[1]}$, C_{2-6}alkenyl, C_{2-6}alkynyl, (C_{3-7}cycloalkyl$_1$)C_{1-4}alkyl$_{[1]}$, (C_{3-7}cycloalkyl$_1$)C_{2-4}alkenyl, (C_{3-7}cycloalkyl$_1$) C_{2-4}alkynyl, -O(C_{3-7}cycloalkyl$_1$)C_{1-4}alkyl$_{[1]}$, -O(C_{3-7}cycloalkyl$_1$)C_{2-4}alkenyl, -O(C_{3-7}cycloalkyl$_1$) C_{2-4}alkynyl, halo(C_{1-6})alkyl$_{[1]}$, haloC_{2-6}alkenyl, haloC_{2-6}alkynyl, -O(halo(C_{1-6})alkyl$_{[1]}$), -O(halo(C_{2-6})alkenyl), -O(halo(C_{2-6})alkynyl), -O(C_{1-6}alkyl$_{[1]}$), -O(C_{2-6}alkenyl), -O(C_{2-6}alkynyl), [and] $S(O)_n$(C_{1-6}alkyl$_{[1]}$, $S(O)_n$(C_{2-6}alkenyl), and $S(O)_n$(C_{2-6}alkynyl),

where each alkyl$_{[1]}$, or alkenyl is independently straight, branched, or cyclic, and each alkynyl is straight or branched, [may contain 1 or more double or triple bonds,] and is optionally substituted with one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino,

and

where each C_{3-7}cycloalkyl$_1$ is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino,

with the proviso that not both R_1 and R_3 are hydrogen;

R_2 is selected from the group consisting of $-XR_A$ and Y; and

Ar is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrimidinyl, pyridizinyl, and thiophenyl, each of which is mono-, di-, or tri-substituted with R_C;

R_A and R_B, which may be the same or different, are independently selected at each occurrence from:

hydrogen, [and] straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, [including] (cycloalkyl)alkyl groups consisting of [1] 3 to 8 carbon atoms, [which] straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, [alkyl groups may contain one or more double or triple bonds,] each of which [1 to 8 carbon atoms] may be further

substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, cyano, amino, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), -NHC(=O)(C_{1-6}alkyl), -N(C_{1-6}alkyl)C(=O)(C_{1-6}alkyl), -NHS(O)$_n$(C_{1-6}alkyl), -S(O)$_n$(C_{1-6} alkyl), -S(O)$_n$NH(C_{1-6}alkyl), -S(O)$_n$N(C_{1-6} alkyl)(C_{1-6}alkyl), and Z;

R_C is independently selected at each occurrence from halogen, cyano, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_D, C_{2-6} alkenyl substituted with 0-2 R_D, C_{2-6}alkynyl substituted with 0-2 R_D, C_{3-7}cycloalkyl substituted with 0-2 R_D, (C_{3-7}cycloalkyl)C_{1-4}alkyl substituted with 0-2 R_D, C_{1-6}alkoxy substituted with 0-2 R_D, -NH(C_{1-6}alkyl) substituted with 0-2 R_D, -N(C_{1-6}alkyl)(C_{1-6}alkyl) each C_{1-6}alkyl independently substituted with 0-2 R_D, -XR_A, and Y;

R_D is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), -S(O)$_n$(alkyl), halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, CO(C_{1-4}alkyl), CONH(C_{1-4}alkyl), CON(C_{1-4}alkyl)(C_{1-4}alkyl), -XR_A, and Y;

X is independently selected at each occurrence from the group consisting of -CH_2-, -CHR_B-, -O-, -C(=O)-, -C(=O)O-, -S(O)$_n$-, -NH-, -NR_B-, -C(=O)NH-, -C(=O)NR_B-, -S(O)$_n$NH-, -S(O)$_n$$NR_B$-, -OC(=S)S-, -NHC(=O)-, -NR_BC(=O)-, -NHS(O)$_n$-, -OSiH_n(C_{1-4}alkyl$_{2-n}$-, and –NR_BS(O)$_n$-;

Y and Z are independently selected at each occurrence from: 3- to 7-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, cyano, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl),and -S(O)$_n$(alkyl),

said 3- to 7-memberered heterocyclic groups containing one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen; and

n is independently selected at each occurrence from 0, 1, and 2.

7. (amended) A compound or salt according to Claim 3, wherein:

Ar is phenyl mono-, di-, or tri-substituted with R_C; and

R_A and R_B, which may be the same or different, are independently selected at each occurrence from:

straight, branched, or cyclic alkyl groups having from 1 to 8 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms [which alkyl groups may contain one or more double or triple bonds].

8. (amended) A compound or salt according to Claim 3, wherein:

Ar is phenyl mono-, di-, or tri-substituted with R_C;

R_A and R_B, which may be the same or different, are independently selected at each occurrence from:

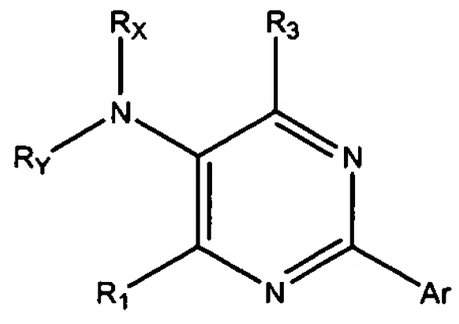
straight, branched, or cyclic alkyl groups having from 1 to 8 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms [which alkyl groups may contain one or more double or triple bonds]; and

R_1 and R_3 are independently selected from the group consisting of

halogen,

C_{-1-3}alkyl, C_{1-3}alkoxy, (C_{3-7}cycloalkyl)C_{1-3}alkyl, (C_{3-7}cycloalkyl) C_{1-3}alkoxy, each of which is unsubstituted or substituted by 1-3 groups independently chosen from hydroxy, amino, cyano, and halogen.

9. (amended) A compound of Formula A



Formula A

or a pharmaceutically acceptable salt thereof, wherein:

R_X and R_Y are the same or different and are independently selected from:

a) hydrogen,

b) -(C=O)alkyl$_A$, wherein alkyl$_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

c) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, [including] cycloalkyl(alkyl)groups[, said alkyl groups having from 1] consisting of 3 to 8 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, [and optionally containing one or more double or triple bonds,] each of which [alkyl groups] may be further substituted with one or more substituent(s) independently selected from:

i) hydroxy, halogen, amino, cyano, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -NH(C_{1-4}alkyl)(C_{1-4}alkyl), and

ii) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents independently selected from halogen, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), –N(C_{1-4}alkyl)(C_{1-4}alkyl), and -S(O)$_n$(alkyl), wherein said 3- to 7-memberered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen,

R_1 and R_3 are independently selected from hydrogen, halogen, cyano, C_{1-6} alkyl$_{[1]}$, C_{2-6}alkenyl, C_{2-6}alkynyl, (C_{3-7}cycloalkyl$_1$)C_{1-4}alkyl$_{[1]}$, (C_{3-7}cycloalkyl$_1$)C_{2-4}alkenyl, (C_{3-7}cycloalkyl$_1$) C_{2-4}alkynyl, -O(C_{3-7}cycloalkyl$_1$)C_{1-4}alkyl$_{[1]}$, -O(C_{3-7}cycloalkyl$_1$)C_{2-4}alkenyl, -O(C_{3-7}cycloalkyl$_1$) C_{2-4}alkynyl, halo(C_{1-6})alkyl$_{[1]}$, haloC$_{2-6}$alkenyl, haloC$_{2-6}$alkynyl, -O(halo(C_{1-6})alkyl$_{[1]}$), -O(halo(C_{2-6})alkenyl), -O(halo(C_{2-6})alkynyl), -O(C_{1-6}alkyl$_{[1]}$), -O(C_{2-6}alkenyl), -O(C_{2-6}alkynyl), [and] S(O)$_n$(C_{1-6}alkyl$_{[1]}$, S(O)$_n$(C_{2-6}alkenyl), and S(O)$_n$(C_{2-6}alkynyl),

where each alkyl$_{[1]}$, or alkenyl is independently straight, branched, or cyclic, and each alkynyl is straight or branched, [may contain 1 or more double or triple bonds,] and is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino,

and

where said C_{3-7}cycloalkyl$_1$ is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino

with the proviso that not both R_1 and R_3 are hydrogen;

Ar is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrimidinyl, and thiophenyl, each of which is mono-, di-, or tri-substituted with R_C;

R_A and R_B, which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, [and] straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, [including] (cycloalkyl)alkyl groups[,] consisting of [1] 3 to 8 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, and straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, [which may contain one or more double or triple bonds,] each of which may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, nitro, cyano, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), -NHC(=O)(C_{1-6}alkyl), -N(C_{1-6}alkyl)C(=O)(C_{1-6}alkyl), -NHS(O)$_n$(C_{1-6}alkyl), -S(O)$_n$(C_{1-6} alkyl), -S(O)$_n$NH(C_{1-6}alkyl), -S(O)$_n$N(C_{1-6} alkyl)(C_{1-6}alkyl), and Z;

R_C is independently selected at each occurrence from halogen, cyano, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, and C_{1-6}alkyl substituted with 0-2 R_D, C_{2-6} alkenyl substituted with 0-2 R_D, C_{2-6}alkynyl substituted with 0-2 R_D, C_{3-7}cycloalkyl substituted with 0-2 R_D, (C_{3-7}cycloalkyl)C_{1-4}alkyl substituted with 0-2 R_D, C_{1-6}alkoxy substituted with 0-2 R_D, -NH(C_{1-6}alkyl) substituted with 0-2 R_D, -N(C_{1-6}alkyl)(C_{1-6}alkyl) each C_{1-4}alkyl independently substituted with 0-2 R_D, -XR_A, and Y, with the proviso that at least one of

the positions ortho or para to the point of attachment of Ar to the pyrimdine ring shown in Formula A is substituted;

R_D is independently selected at each occurrence the group consisting of halogen, hydroxy, cyano, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), -S(O)$_n$(alkyl) halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, CO(C_{1-4}alkyl), CONH(C_{1-4}alkyl), CON(C_{1-4}alkyl)(C_{1-4}alkyl), -XR_A, and Y;

X is independently selected at each occurrence from the group consisting of -CH_2-, -CHR_B-, -O-, -C(=O)-, -C(=O)O-, -S(O)$_n$-, -NH-, -NR_B-, -C(=O)NH-, -C(=O)NR_B-, -S(O)$_n$NH-, -S(O)$_n$$NR_B$-, -OC(=S)S-, -NHC(=O)-, -NR_BC(=O)-, -NHS(O)$_n$-, -OSiH_n(C_{1-4}-alkyl$_{2-n}$)-, and –NR_BS(O)$_n$-;

Y and Z are independently selected at each occurrence from the group consisting of: 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), and -S(O)$_n$(alkyl); and

n is 0, 1, or 2.

10. (amended) A compound or salt according to Claim 9, wherein:

R_X and R_Y are the same or different and are independently selected from:

a) -(C=O)alkyl$_A$, wherein alkyl$_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

b) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, [including] (cycloalkyl)alkyl groups[,] consisting of [said alky groups having from 1] 3 to 8 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms [and optionally containing one or more double or triple bonds], each of which [alkyl groups] may be further substituted with one or more substituent(s) independently selected from:

i) hydroxy, halogen, amino, cyano, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -NH(C_{1-4}alkyl)(C_{1-4}alkyl), and

ii) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents independently selected from halogen, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), –N(C_{1-4}alkyl)(C_{1-4}alkyl), and -S(O)$_n$(alkyl), wherein said 3- to 7-memberered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen,

R_1 and R_3 are independently selected from hydrogen, halogen, cyano, C_{1-6} alkyl$_{[1]}$, C_{2-6}alkenyl, C_{2-6}alkynyl, (C_{3-7}cycloalkyl$_1$)C_{1-4}alkyl$_{[1]}$, (C_{3-7}cycloalkyl$_1$)C_{2-4}alkenyl, (C_{3-7}cycloalkyl$_1$) C_{2-4}alkynyl, -O(C_{3-7}cycloalkyl$_1$)C_{1-4}alkyl$_{[1]}$, -O(C_{3-7}cycloalkyl$_1$)C_{2-4}alkenyl, -O(C_{3-7}cycloalkyl$_1$) C_{2-4}alkynyl, halo(C_{1-6})alkyl$_{[1]}$, haloC$_{2-6}$alkenyl, haloC$_{2-6}$alkynyl, -O(halo(C_{1-6})alkyl$_{[1]}$), -O(halo(C_{2-6})alkenyl), -O(halo(C_{2-6})alkynyl), [and] -O(C_{1-6}alkyl$_{[1]}$), -O(C_{2-6}alkenyl), and -O(C_{2-6}alkynyl),

where each [said] alkyl$_{[1]}$, or alkenyl is independently straight, branched, or cyclic, and each alkynyl is straight or branched, [may contain 1 or more double or triple bonds,] and is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino,

and

where said C_{3-7}cycloalkyl$_1$ is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino

Ar is phenyl, which is mono-, di-, or tri-substituted with R_C;

R_A and R_B, which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, [and] straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, [including] (cycloalkyl)alkyl groups[,] consisting of [1] 3 to 8 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, and

straight or branched alkynyl groups consisting of 2 to 8 carbon atoms [which may contain one or more double or triple bonds], each of which may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, nitro, cyano, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), -NHC(=O)(C_{1-6}alkyl), -N(C_{1-6}alkyl)C(=O)(C_{1-6}alkyl), and Z;

R_C is independently selected at each occurrence from halogen, cyano, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, and C_{1-6}alkyl substituted with 0-2 R_D, C_{2-6} alkenyl substituted with 0-2 R_D, C_{2-6}alkynyl substituted with 0-2 R_D, C_{3-7}cycloalkyl substituted with 0-2 R_D, (C_{3-7}cycloalkyl)C_{1-4}alkyl substituted with 0-2 R_D, C_{1-6}alkoxy substituted with 0-2 R_D, -NH(C_{1-6}alkyl) substituted with 0-2 R_D, -N(C_{1-6}alkyl)(C_{1-6}alkyl) each C_{1-4}alkyl independently substituted with 0-2 R_D, -XR_A, and Y, with the proviso that at least one of the positions ortho or para to the point of attachment of Ar to the pyrimidine ring shown in Formula A is substituted;

R_D is independently selected at each occurrence the group consisting of halogen, hydroxy, cyano, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, CO(C_{1-4}alkyl), CONH(C_{1-4}alkyl), CON(C_{1-4}alkyl)(C_{1-4}alkyl), -XR_A, and Y;

X is independently selected at each occurrence from the group consisting of -CH_2-, -CHR_B-, -O-, -C(=O)-, -C(=O)O-, -NH-, -NR_B-, -C(=O)NH-, -C(=O)NR_B-, -NHC(=O)-, and -NR_BC(=O)-;

Y and Z are independently selected at each occurrence from the group consisting of: 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -N(C_{1-4}alkyl)(C_{1-4}alkyl); and

n is 0,1, or 2.

13. (amended) A compound or salt according to claim 9, wherein:

Ar is phenyl mono-, di-, or tri-substituted with R_C,

R_X and R_Y, which may be the same or different, are independently selected at each occurrence from

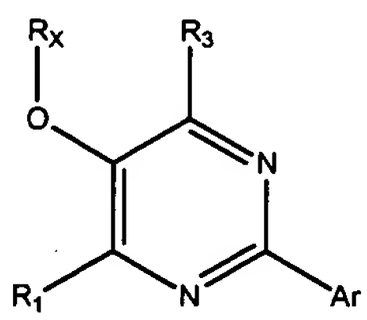
straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, [including] (cycloalkyl)alkyl groups[,] consisting of [1] 3 to 8 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, [which may contain one or more double or triple bonds]; and

R_1 and R_3 are independently selected from the group consisting of hydrogen, halogen, C_{1-4}alkoxy, halo(C_{1-4})alkyl, (halo(C_{1-4})alkoxy,

C_{1-6}alkyl, which C_{1-6}alkyl is unsubstituted or substituted by one to three substituents independently selected from hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino,

(C_{3-7}cycloalkyl)C_{1-4}alkyl, which (C_{3-7}cycloalkyl)C_{1-4}alkyl is unsubstituted or substituted by one to three substituents independently selected from hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino.

15. (amended) A compound or salt according to claim 3, of the formula



wherein:

R_X is chosen from

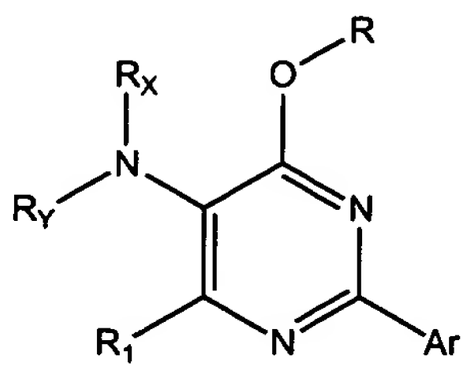
straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, [including] (cycloalkyl)alkyl groups[,] consisting of [having from 1] 3 to 8 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms [which may contain one or

more double or triple bonds], each of which may be further substituted with one or more substituent(s) independently selected from:

(a) hydroxy, halogen, amino, cyano, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -NH(C_{1-4}alkyl)(C_{1-4}alkyl), and

(b) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substitutents selected from halogen, halo(C_{1-4})alkyl, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), –N(C_{1-4}alkyl)(C_{1-4}alkyl), wherein said 3- to 7-memberered heterocyclic groups contain one or more heteroatom(s) selected from N, O, and S, with the point of attachment being either carbon or nitrogen.

17. (amended) A compound or salt according to Claim 3 of Formula B:



FORMULA B

Ar is phenyl mono-, di-, or tri-substituted with R_C;

R is selected from straight, branched, or cyclic alkyl groups, [including] (cycloalkyl)alkyl groups, <u>straight, branched, or cyclic alkenyl groups, or straight or branched alkynyl groups</u> [which may contain 1 or more double or triple bonds], and which are optionally substituted by one or more substituents independently chosen from oxo, hydroxy, halogen, cyano, -O(C_{1-4} alkyl), amino, -NH(C_{1-4} alkyl), and -N(C_{1-4} alkyl)(C_{1-4} alkyl);

R_1 is selected from hydrogen, [halogen]<u>bromo, fluoro, iodo</u>, cyano, C_{1-4} alkyl, (C_{3-7}cycloalkyl)C_{1-4}alkyl, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, and -O(C_{1-4}alkyl); and

R_X and R_Y are the same or different and are independently selected from:

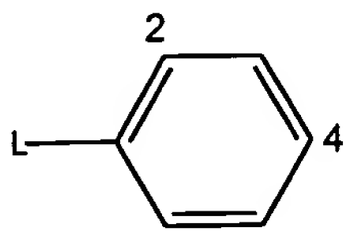
a) hydrogen,

b) -(C=O)alkyl$_A$, wherein alkyl$_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

c) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, [including] (cycloalkyl)alkyl groups[, having from 1] consisting of 3 to 8 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms [which may contain one or more double or triple bonds], each of which may be further substituted with one or more substituent(s) independently selected from (i)hydroxy, halogen, amino, cyano, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -NH(C_{1-4}alkyl)(C_{1-4}alkyl), and (ii)3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substitutents selected from halogen, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), –N(C_{1-4}alkyl)(C_{1-4}alkyl), and -S(O)$_n$(alkyl), wherein said 3- to 7-memberered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen.

19. (amended) A compound or salt according to Claim 17, wherein

Ar is a phenyl group of the formula:



wherein L indicates a bond to the pyrimidine ring in Formula B

and the Ar phenyl group is substituted at one, two, or three of positions 2, 4, and 6 with substituents independently selected from:

i) halogen, cyano, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, hydroxy, amino, C_{1-6} alkyl, C_{1-6}alkoxy, (C_{1-4}alkoxy)C_{1-4}alkoxy, and mono- or di(C_{1-4}alkyl)amino,

ii) C_{1-6} alkyl and C_{1-6}alkoxy which are further substituted with a 3- to 7-membered carbocyclic and heterocyclic group, which is saturated, unsaturated, or aromatic, which 3- to 7-

membered carbocyclic and heterocyclic group may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -N(C_{1-4}alkyl)(C_{1-4}alkyl);

R_X and R_Y are the same or different and are independently selected from the group consisting of:

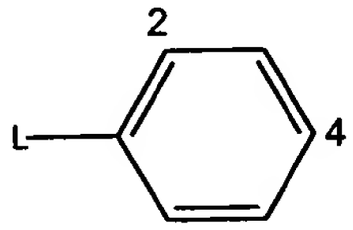
a) hydrogen (with the proviso that R_x and R_Y are not both hydrogen),

b) -(C=O)$alkyl_A$, wherein $alkyl_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

c) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, [including] (cycloalkyl)alkyl[,] groups consisting of 3 to 8 carbon atoms, [said] straight, branched, or cyclic [alkyl having from 1] alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, [and containing zero, one or more double or triple bonds, each of] which [1 to 8 carbon atoms] may be further substituted with one or more substituent(s) independently selected from hydroxy, halogen, amino, cyano, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -NH(C_{1-4}alkyl)(C_{1-4}alkyl).

20. (amended) A compound or salt according to Claim 17, wherein

Ar is a phenyl group of the formula:



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wherein L indicates a bond to the pyrimidine ring in Formula B

and the Ar phenyl group is substituted at one, two, or three of positions 2, 4, and 6 with substituents independently selected from:

i) halogen, cyano, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, hydroxy, amino, C_{1-6} alkyl, C_{1-6}alkoxy, (C_{1-4}alkoxy)C_{1-4}alkoxy, and mono- or di(C_{1-4}alkyl)amino,

ii) C_{1-6} alkyl and C_{1-6}alkoxy which are further substituted with a 3- to 7-membered carbocyclic and heterocyclic group, which is saturated, unsaturated, or aromatic, which 3- to 7-membered carbocyclic and heterocyclic group may be further substituted with one or more

substituents independently selected from halogen, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -N(C_{1-4}alkyl)(C_{1-4}alkyl);

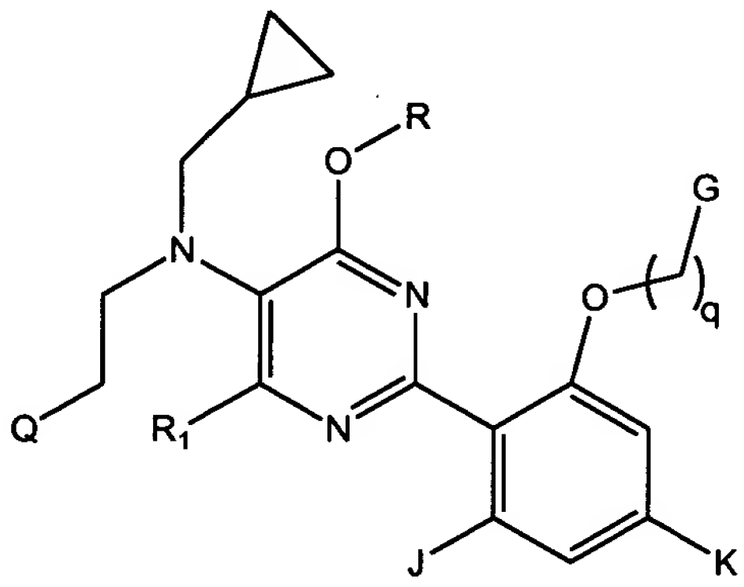
R_X and R_Y are the same or different and are independently selected from the group consisting of:

a) hydrogen (with the proviso that R_x and R_Y are not both hydrogen),

b) -(C=O)$alkyl_A$, wherein $alkyl_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

c) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, [including] (cycloalkyl)alkyl groups consisting of 3 to 8 carbon atoms, [said] straight, branched, or cyclic [alkyl] alkenyl groups [have from] consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms [and may contain one or more double or triple bonds].

22. (amended) A compound or salt according to Claim 17, of the formula:



wherein:

Q is hydrogen, C_{3-7} cycloalkyl, pyrrolidinyl, piperidinyl, morpholino, or piperazinyl;

q is an integer from 1 to 4;

G is hydrogen, hydroxy, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), or a 3- to 7-membered carbocyclic or heterocyclic group, which is saturated, unsaturated, or aromatic, which is unsubstituted or substituted with one or more substituents independently selected from halogen, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), –N(C_{1-4}alkyl)(C_{1-4}alkyl), and -$S(O)_n$(alkyl), wherein said 3- to 7-memberered heterocyclic group contains one or more

heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen;

J and K are independently selected from halogen, cyano, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, hydroxy, amino, C_{1-6} alkyl, C_{1-4}alkyl, C_{1-4}alkoxy, (C_{1-4}alkoxy) C_{1-4}alkoxy, and mono- or di(C_{1-4}alkyl)amino; and

R_X and R_Y are the same or different and are independently selected from hydrogen (with the proviso that R_X and R_Y are not both hydrogen), [and] straight, branched, or cyclic alkyl groups having from 1 to 6 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 6 carbon atoms, and straight or branched alkynyl groups consisting of 2 to 6 carbon atoms, [which alkyl groups may contain one or more double or triple bonds].